IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Pavak R. MEHTA et al. Art Unit: 1615

Application No.: 10/599,907 Examiner: Humera N. Sheikh

Filed: October 13, 2006

For: DOSAGE FORM HAVING POLYMORPHIC STABILITY

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

REQUEST FOR RECONSIDERATION

In response to the Office Action dated October 29, 2010 for the above-identified application, consideration of the following remarks is requested.

Claims 1-23 remain pending in this application. All of the claims have been rejected on various grounds, which will be discussed separately below.

A. Rejections Under 35 U.S.C. § 102(e)

1. Claims 1, 2, and 6-8 stand rejected under this statute, it being asserted that they are anticipated by U.S. Patent Application Publication No. 2003/0129250 of Batycky et al. ("Batycky"). This publication teaches the preparation, by spray-drying, of solubility-enhanced particles containing poorly soluble drugs. Dilute drug solutions, containing excipients such as surfactants, "matrix builders," and stabilizers, are spray-dried to produce particles having small sizes, high surface areas, and thin walls, where the drug (reportedly amorphous) is embedded in regions of the walls. As pointed out in the Office Action, Batycky states that the particles can be compressed about 10 to about 29 times, and will retain their drug dissolution rates (page 3, paragraph 0031).

The presently rejected claims (as represented by independent claim 1) pertain to pharmaceutical dosage forms containing a drug that is susceptible to polymorphic conversion, prepared by compressing using low enough forces to preserve the original

polymorphic form. This is significantly different from any teachings of Batycky, which does not contain any mention of polymorphic form conversion problems. In fact, the spray-dried particles prepared by Batycky are said to not change their dissolution properties upon compression, at least implying that they would not qualify as the Applicants' required drug substance that is susceptible to polymorphic form conversion. Batycky does not describe the polymorphic forms that exist following its contemplated compression operation, and the Office Action statement (page 4, fourth paragraph) that its drugs are subject to polymorphic conversion cannot be considered as being correct, in view of the plain teachings regarding unchanged solubility and the absence of any information about polymorphic forms after compression.

It should further be noted that the present claim 1 applies to using a drug substance in any polymorphic form, crystalline or amorphous, and Batycky certainly does not contain teachings that would apply to making a dosage form using a crystalline drug.

Anticipation is established by the presence of teachings in a prior art document that describe every element of a claim, with the elements being arranged as in the claim. *In re Hyatt*, 211 F.3d 1367, 54 USPQ2d 1664 (Fed. Cir. 2000) and *Richardson v. Suzuki Motor Co.*, 868 F.2d1226, 9 USPQ2d 1913 (Fed. Cir. 1989). As discussed above, claim 1 is not anticipated since it requires a drug substance that is subject to polymorphic conversion, and there is no evidence that drug particles in Batycky are subject to such conversions during compression. Further, the publication does not discuss any particular conditions for compression (as acknowledged in the Office Action on page 8, first paragraph), so that claim limitation is not disclosed. Rejected claims 2 and 6-8, being dependent from claim 1, also cannot be anticipated.

This rejection should not be maintained, after reconsideration.

2. Claims 1-3 and 8 stand rejected under this statute, it being asserted that they are anticipated by U.S. Patent Application Publication No. 2003/0104063 of Babcock et al. ("Babcock"). Babcock teaches amorphous drug-matrix dispersion compositions, formulated together with a "concentration-enhancing" polymer to provide increased solubility and bioavailability. On page 62, in paragraph 1241, the dispersed drug is said to have physical stability, i.e., that it remains in an amorphous or crystalline state.

Applicants submit that this stabilized dispersion would not be a drug that is susceptible to polymorphic conversion, in the context of their claimed invention. Therefore, it cannot be said that the publication teaches this claim limitation. In addition, there are no teachings in the document about compression parameters, although tablets are mentioned at page 72 in a list of dosage forms, in paragraph 1316. Since the limitations of claim 1 are not taught in the publication, that claim and its dependent claims 2, 3, and 8 cannot possibly be anticipated under current legal standards.

Reconsideration and withdrawal of this rejection are requested.

A. Rejections Under 35 U.S.C. § 103(a)

Applicants point to the discussion of the standards for obviousness discussed on page 6 of the Office Action, particularly the second *Graham v. John Deere Co.* factual inquiry. The focus must be on differences between the cited documents and the claims, to determine whether the invention would have been obvious to a person having ordinary skill in the art.

1. Claims 1, 3-5, and 9-20 were rejected under this statute as being rendered obvious by Batycky. The teachings of this publication are discussed above, in the context of anticipation, and significant differences were noted between those teachings and the limitations of claim 1. A rejection for obviousness could be proper only if those differences can somehow be supplied by the state of the art, and Applicants respectfully submit that this is not possible.

Batycky shows the formation of an amorphous combination of a drug and a matrix, using spray drying. If this combination is used to make a pharmaceutical dosage form, it cannot be said to constitute the use of a drug substance that is susceptible to polymorphic conversion, as is required by claim 1. What Batycky teaches perhaps could be an alternative to using the claimed invention, albeit a more complicated alternative.

The Office Action stated that the determination of suitable or effective compression forces can be done using routine experimentation. This statement is the result of an impermissible hindsight analysis, since there is nothing in the art of record to suggest that compression force has any effect on drug polymorphic conversion in a

dosage form. Whether or not something is "possible" is not relevant to the question, as obviousness requires establishment of a likelihood that a person having ordinary skill in the art would have been led to make the claimed invention.

The Office Action further stated that tablet dimensions, specified in dependent claims 13, 15, and 19, are shown in Batycky. However, this is not correct. The claim limitations "about 3 mm" and "about 1 mm to about 3 mm" simply are not the same as the document's teachings of powder particle sizes about 5 to about 50 μm. Applicants' compressed mini-tablets are hundreds of times larger than the document's powder particles.

The Office Action further stated that, regarding instant claim 9, Batycky teaches mixing an active agent with one or more excipients. This is not correct, in the context of Applicants' claimed invention, since the Batycky teachings relate to combining a particular composition containing a drug substance and other components (and prepared by spray-drying), with excipients. Applicants' claims all require that the drug substance is one that is susceptible to polymorphic conversion, and nothing in the specification alludes to that drug substance being a component of some type of composition such as is prepared by Batycky.

Therefore, any conclusion that the rejected claims are *prima facie* obvious is not correct, and the rejection should be withdrawn upon reconsideration.

2. Claims 21-23 were rejected under this statute, as being rendered obvious by the previously discussed Batycky publication, in view of teachings in U.S. Patent Application Publication No. 2008/0119654 of Khanna et al. ("Khanna").

Khanna teaches an amorphous form of esomeprazole salts, prepared by removing the solvent from solutions of the salts. Examples show spray-drying procedures for preparation of an amorphous drug, starting from esomeprazole magnesium trihydrate. There is no information regarding procedures for using the amorphous drug to prepare a dosage form, although the specification (page 2, paragraph 0031) states that it can be used to make "ordinary dosage forms."

The teachings of Khanna do not overcome the significant differences, previously discussed, between the Applicants' claims and teachings of Batycky. Claims 21-23 depend from claim 1, directly or indirectly, and therefore contain all of the limitations of

claim 1. Please note that claims 21-23 do not specify the use of amorphous esomeprazole magnesium.

All that can be said about the Khanna publication is that it discloses one or more amorphous forms of esomeprazole magnesium, or hydrates or solvates thereof. We cannot know whether the disclosed amorphous forms will be polymorphically stable or unstable, during their formulation into a pharmaceutical dosage form. Therefore, the relevance of the publication to the Applicants' claims has not been established.

Moreover, any possible combinations of the two cited publications will not meet the limitations of the rejected claims. Substituting the amorphous esomeprazole prepared in Khanna for the starting drugs in Batycky still gives a product of Batycky. As discussed previously, there is no *prima facie* case for obviousness.

CONCLUSION

The rejections under 35 U.S.C. § 102(e) and 103(a) have been shown to not have a proper scientific or legal foundation. Therefore, reconsideration and withdrawal of the rejections are respectfully requested.

If any minor matters remain to be resolved before the claims are allowed, please contact the undersigned directly to obtain a prompt resolution.

Respectfully submitted,

/R. A. Franks/

Robert A. Franks
Reg. No. 28,605
Attorney for Applicants

January 28, 2011

Dr. Reddy's Laboratories, Inc.
200 Somerset Corporate Blvd., Seventh Floor
Bridgewater, New Jersey 08807-2862
Telephone: 908-203-6504
Facsimile: 908-203-6515